

Amendments to the Specification:

Please replace the paragraphs beginning at page 13, lines 15-30, with the following:

- (i) cyclizing the N-terminal amine with the C-terminal carboxyl acid function, either directly via an amide bond between the N-terminal nitrogen and C-terminal carbonyl, or indirectly via a spacer group, for example by condensation with an **M-amino N-amino** carboxylic acid;
- (ii) cyclizing via the formation of a covalent bond between the side chains of two residues, such as an amide bond between a lysine residue and either an aspartic acid or glutamic acid residue, or a disulfide bond between two cysteine residues, or a thioether bond between a cysteine residue and ~~an~~ **halogenated a halogenated** amino acid residue, either directly or via a spacer group as described in (i) above. The residues contributing the side chains may be derived from the B-chain sequence itself, or may be incorporated into or added on to the B-chain sequence for this purpose; and,
- (iii) cyclizing via the formation of an amide bond between a side chain (for example of a lysine or aspartate residue) and either the C-terminal carboxyl or N-terminal amine, either directly or using a spacer group as described in (i) above. The residues contributing the side chains may be derived from the B-chain sequence itself, or may be incorporated into or added on to the B-chain sequence for this purpose.